



SEQUENCE LISTING

<110> KISHIMOTO, TADAMITSU
MIHARA, MASAHIKO
MORIYA, YOICHIRO
OSHUGI, YOSIYUKI

<120> CHRONIC RHEUMATOID ARTHRITIS THERAPY CONTAINING IL-6
ANTAGONIST AS EFFECTIVE COMPONENT

<130> 053466/0296

<140> 09/756,125

<141> 2001-01-09

<150> 09/233,474

<151> 1999-01-20

<150> 08/817,084

<151> 1997-04-07

<150> PCT/JP95/01144

<151> 1995-06-07

<150> 08/971,997

<151> 1997-02-21

<150> 08/268,520

<151> 1994-06-30

<150> JP 6-244035

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atattctcta gagagattct

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Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn

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5

10

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Tyr Thr Ser Arg Leu His Ser
1 5

<210> 4
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Gln Gln Gly Asn Thr Leu Pro Tyr Thr
1 5

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
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Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
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Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr
1 5 10 15

Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys
20 25 30

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Ser Asp His Ala Trp Ser
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Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser
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Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr
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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr
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Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly
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Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser Leu Arg
1 5 10 15
Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

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Trp Gly Gln Gly Ser Leu Val Thr Val Ser Ser
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| aagcttccac | c | atg | gga | tgg | agc | tgt | atc | atc | ctc | ttc | ttg | gta | gca | aca | 50 |
| | Met | Gly | Trp | Ser | Cys | Ile | Ile | Leu | Phe | Leu | Val | Ala | Thr | | |
| | 1 | | | | 5 | | | | | 10 | | | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|
| gct | aca | ggt | gtc | cac | tcc | cag | gtc | caa | ctg | cag | gag | agc | ggt | cca | ggt | 98 |
| Ala | Thr | Gly | Val | His | Ser | Gln | Val | Gln | Leu | Gln | Glu | Ser | Gly | Pro | Gly | |
| | 15 | | | | | 20 | | | | | 25 | | | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| ctt | gtg | aga | cct | agc | cag | acc | ctg | agc | ctg | acc | tgc | acc | gtg | tct | ggc | 146 |
| Leu | Val | Arg | Pro | Ser | Gln | Thr | Leu | Ser | Leu | Thr | Cys | Thr | Val | Ser | Gly | |
| 30 | | | | | 35 | | | | | 40 | | | | | 45 | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| tac | tca | att | acc | agc | gat | cat | gcc | tgg | agc | tgg | gtt | cgc | cag | cca | cct | 194 |
| Tyr | Ser | Ile | Thr | Ser | Asp | His | Ala | Trp | Ser | Trp | Val | Arg | Gln | Pro | Pro | |
| | | | | 50 | | | | | 55 | | | | | 60 | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| gga | cga | ggt | ctt | gag | tgg | att | gga | tac | att | agt | tat | agt | gga | atc | aca | 242 |
| Gly | Arg | Gly | Leu | Glu | Trp | Ile | Gly | Tyr | Ile | Ser | Tyr | Ser | Gly | Ile | Thr | |
| | | | 65 | | | | | 70 | | | | | 75 | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| acc | tat | aat | cca | tct | ctc | aaa | tcc | aga | gtg | aca | atg | ctg | aga | gac | acc | 290 |
| Thr | Tyr | Asn | Pro | Ser | Leu | Lys | Ser | Arg | Val | Thr | Met | Leu | Arg | Asp | Thr | |
| | | 80 | | | | | 85 | | | | | 90 | | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| agc | aag | aac | cag | ttc | agc | ctg | aga | ctc | agc | agc | gtg | aca | gcc | gcc | gac | 338 |
| Ser | Lys | Asn | Gln | Phe | Ser | Leu | Arg | Leu | Ser | Ser | Val | Thr | Ala | Ala | Asp | |
| | 95 | | | | | 100 | | | | | 105 | | | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| acc | gcg | gtt | tat | tat | tgt | gca | aga | tcc | cta | gct | cgg | act | acg | gct | atg | 386 |
| Thr | Ala | Val | Tyr | Tyr | Cys | Ala | Arg | Ser | Leu | Ala | Arg | Thr | Thr | Ala | Met | |
| 110 | | | | | 115 | | | | | 120 | | | | | 125 | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------------|-----|--|--|
| gac | tac | tgg | ggt | caa | ggc | agc | ctc | gtc | aca | gtc | tcc | tca | ggtgagtgga | 435 | | |
| Asp | Tyr | Trp | Gly | Gln | Gly | Ser | Leu | Val | Thr | Val | Ser | Ser | | | | |
| | | | | 130 | | | | | | 135 | | | | | | |

| | | | | | | | | | | | | | | | | |
|-----|--|--|--|--|--|--|--|--|--|--|--|--|--|--|--|-----|
| tcc | | | | | | | | | | | | | | | | 438 |
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<211> 138

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| Met | Gly | Trp | Ser | Cys | Ile | Ile | Leu | Phe | Leu | Val | Ala | Thr | Ala | Thr | Gly |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Val | His | Ser | Gln | Val | Gln | Leu | Gln | Glu | Ser | Gly | Pro | Gly | Leu | Val | Arg |
| | | | 20 | | | | | 25 | | | | | 30 | | |

Pro Ser Gln Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile

| | | |
|---|-----|-----|
| 35 | 40 | 45 |
| Thr Ser Asp His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly | | |
| 50 | 55 | 60 |
| Leu Glu Trp Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn | | |
| 65 | 70 | 75 |
| Pro Ser Leu Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn | | |
| | 85 | 90 |
| Gln Phe Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val | | |
| | 100 | 105 |
| Tyr Tyr Cys Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp | | |
| | 115 | 120 |
| Gly Gln Gly Ser Leu Val Thr Val Ser Ser | | |
| 130 | 135 | |

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<220>
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| aagcttccac c atg gga tgg agc tgt atc atc ctc ttc ttg gta gca aca | 50 |
| Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr | |
| -15 -10 | |
| gct aca ggt gtc cac tcc gac atc cag atg acc cag agc cca agc agc | 98 |
| Ala Thr Gly Val His Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser | |
| -5 -1 1 5 10 | |
| ctg agc gcc agc gtg ggt gac aga gtg acc atc acc tgt aga gcc agc | 146 |
| Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser | |
| 15 20 25 | |

| | |
|---|-----|
| cag gac atc agc agt tac ctg aat tgg tac cag cag aag cca gga aag | 194 |
| Gln Asp Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys | |
| 30 35 40 | |
| | |
| gct cca aag ctg ctg atc tac tac acc tcc aga ctg cac tct ggt gtg | 242 |
| Ala Pro Lys Leu Leu Ile Tyr Tyr Thr Ser Arg Leu His Ser Gly Val | |
| 45 50 55 | |
| | |
| cca agc aga ttc agc ggt agc ggt agc ggt acc gac ttc acc ttc acc | 290 |
| Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr | |
| 60 65 70 | |
| | |
| atc agc agc ctc cag cca gag gac atc gct acc tac tac tgc caa cag | 338 |
| Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln | |
| 75 80 85 90 | |
| | |
| ggt aac acg ctt cca tac acg ttc ggc caa ggg acc aag gtg gaa atc | 386 |
| Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile | |
| 95 100 105 | |
| | |
| aaa cgtgagtgga tcc | 402 |
| Lys | |

<210> 20
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 <213> Artificial Sequence

<220>
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Val His Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
 -1 1 5 10

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile
 15 20 25

Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
 30 35 40 45

Leu Leu Ile Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg
 50 55 60

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser
 65 70 75

Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr
 80 85 90

Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
95 100 105